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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,989	11/21/2003	Xuedong Song	KCX-741 (19044)	9109
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DORITY & MANNING, P.A. POST OFFICE BOX 1449 GREENVILLE, SC 29602-1449			EXAMINER DIRAMIO, JACQUELINE A	
			ART UNIT 1641	PAPER NUMBER
			MAIL DATE 05/29/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,989	SONG, XUEDONG	
	Examiner	Art Unit	
	Jacqueline DiRamio	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 64-85 and 87-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64-85 and 87-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

The amendments to claims 64, 76, 77 and 85 are acknowledged, as well as the cancellation of claim 86 and the addition of new claims 89 – 92.

Currently, claims 64 – 85 and 87 – 92 are pending and under examination.

Withdrawn Objections and Rejections

The previous objection to claim 77 is withdrawn in view of Applicant's amendments filed March 15, 2007.

All previous claim rejections under 35 U.S.C. 103 are withdrawn in view of Applicant's amendments and arguments filed March 15, 2007.

Response to Arguments

Applicant's arguments, see p6-11, filed March 15, 2007, with respect to the rejection(s) of the claim(s) under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of O'Riordan et al. (*Anal. Chem.*, **74** (2002) 5845-5850), and further in view of Klimant (US 6,770,22) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration of the Klimant reference, a new ground(s) of rejection is made and presented below.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 64 – 77, 79, 80, 82 – 84, 87 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), and in light of O’Riordan et al. (“Monofunctional Derivatives of Coproporphyrins for Phosphorescent Labeling of Proteins and Binding Assays,” *Anal. Biochem.* **290** (2001) 366-375).

Daniels et al. teach a method for detecting an analyte within a test sample, the method comprising:

i) providing a lateral flow test strip (assay device) that comprises a porous membrane in fluid communication with semiconductor nanocrystals (luminescent or phosphorescent particles) conjugated with a specific binding member, wherein the

Art Unit: 1641

porous membrane defines a capture region (detection zone) within which is immobilized a capture reagent;

ii) contacting the lateral flow test strip with the test sample;

iii) subjecting the capture region to illumination to generate a detection signal;

and

iv) thereafter, measuring the intensity of the detection signal, wherein the amount of the analyte within the test sample is proportional to the intensity of the detection signal (see Figure 1; and paragraphs [0016]-[0028], [0079]-[0082], [0095], [0109], [0111], [0115]-[0120], [0126]-[0128], [0170], and [0212]-[0215]).

However, Daniels et al. fail to teach that the luminescent/phosphorescent particle comprises a phosphorescent label encapsulated within a matrix and that the label has an emission lifetime of about 1 microsecond or more.

Klimant teaches of the production and use of luminescent microparticles wherein long-lived phosphorescent labels are incorporated (encapsulated) within solid particles for use as internal standards for referencing phosphorescence signals or as markers for labeling and detecting biomolecules (see column 1, lines 1-16). Luminescence measurements using phosphorescence signals is a very common method in biological and chemical analysis due to its high sensitivity and versatility (see column 1, lines 30-35). The incorporation of the phosphorescence labels within matrices allows for elimination or great reduction in phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement (see column 1, lines 17-23).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine with the detection method of Daniels et al. the luminescent microparticles taught by Klimant because Klimant teaches the benefit of luminescent microparticles that comprise phosphorescence labels encapsulated within matrices because the microparticles create long-lived luminescence, wherein the matrices eliminate or greatly reduce phosphorescence signal quenching by interfering oxygen that is common during luminescence measurement.

With respect to Applicant's recitation in claim 64 of the phosphorescent label having an emission lifetime of about 1 microsecond or more, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyrin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of 1 microsecond or more (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claims 65, 66, and 68, Klimant teaches that the phosphorescent label is a metal/ligand complex, particularly comprised of transition metals such as ruthenium, osmium, iridium, rhenium, platinum, or palladium, and also containing complex ligands, such as **bipyridine**, bipyrazine, phenanthroline, terpyridil or derivatives thereof (see column 3, lines 14-21).

With respect to Applicant's claims 67 and 69, Klimant teaches the phosphorescent label can further comprise a porphyrin ligand or porphyrin complex with platinum(II) or palladium(II), which anticipates Applicant's claims 7 and 31 because the

porphyrin complexes encompass the derivatives and combinations thereof and are being utilized for the same purpose (see column 3, lines 25-31).

With respect to Applicant's claim 70, Klimant teaches the matrix incorporating the phosphorescent label comprises polymer particles (see column 4, lines 11-19).

With respect to Applicant's claims 71 and 72, Klimant teaches the size of the luminescent particles in the range of 20 μm to 10 μm , particularly from 50 nm to 1 μm (see column 3, lines 37-39).

With respect to Applicant's claim 73, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching (see column 1, lines 17-23).

With respect to Applicant's claims 74 and 75, Klimant teaches the matrix incorporating the phosphorescent label protects the label from quenching, enabling the luminescence lifetime (detection signal) to be only 20%, at most 15% and preferably at most 10% shorter than in an O_2 free environment, which anticipates Applicant's claims 74 and 75 (see column 3, lines 5-13).

With respect to Applicant's claims 76 and 77, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyrin complexes of Pt(II) or Pd(II), which are known in the art to have emission lifetimes of up to 1000 microseconds (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

With respect to Applicant's claim 79, Daniels et al. teach that the capture reagent in the capture region comprises a specific binding member, such as an antigen, hapten, antibody, or streptavidin (see Figures 1 and 2; and paragraphs [0025], [0088]-[0090], and [0116]).

With respect to Applicant's claim 80, Daniels et al. teach that the illumination source can be a pulsed excitation source (see paragraph [0170]).

With respect to Applicant's claims 82-84, Daniels et al. teach that the specific binding member that is conjugated to the luminescent particles, i.e. semiconductor nanocrystals, is configured to preferentially bind with the analyte and can comprise antigens, haptens, aptamers, and antibodies, as well as analogs of the analyte itself (see paragraphs [0016], [0024], [0088]-[0090], and [0094]-[0098]).

With respect to Applicant's claims 87 and 88, the phosphorescent labels used by Klimant preferably comprise metal/ligand complexes that include porphyrin complexes of Pt(II) or Pd(II), which are known in the art to have Stokes shift of 100 nm or more (see Klimant: column 3, lines 14-36; and O'Riordan et al.: p366).

Claims 78 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Zarling et al. (US 5,674,698).

The Daniels et al. and Klimant references, which were discussed in the 103(a) rejection above, fail to teach that the detection signal is measured from 1 to 100 microseconds after the detection zone is subjected to one or more pulses of illumination, or that the signal is measured by a time-gated detector.

Zarling et al. teach of up-converting and down-converting phosphorescent/luminescent reporters for use in biological assays using laser excitation techniques. The detection and quantitation of the phosphorescent reporters is

accomplished by illuminating the sample suspected of containing the reporters and detecting the phosphorescent radiation at more or more emission bands. Various means can be used for detection of the phosphorescent emission(s), including a time-gated and/or frequency-gated light detector for rejection of residual background noise. Time-gated detection is desirable because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected. A pulsed excitation source is preferable for use with a time-gated detector, wherein the phosphorescent reporters have emission lifetimes on the order of 1 ms (see Abstract; column 1, lines 12-18; column 31, lines 50-56; column 32, lines 54-67; and column 33, lines 1-18).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant the use of a pulsed excitation source and time-gated detection, wherein the detection signal is measured a certain time period after the excitation as taught by Zarling et al. because Zarling et al. teach the advantages of using a pulsed excitation source and time-gated detection with phosphorescent labels because it provides a method of recording long-lived emission after termination of illumination, wherein signal(s) attributable to phosphorescence is recorded, while short-lived autofluorescence and scattered illumination light is rejected.

Claims 85 and 89 – 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220), as applied to claim 64 above, and further in view of Rylatt et al. (WO 97/009620).

Daniels et al. teach an additional control line or region, but fail to teach that the control line works as a calibration zone, wherein the intensity of the detection signal is calibrated by the intensity of the calibration signal. Klimant also fails to teach the use of a calibration zone.

Rylatt et al. teach a method for quantitative determination of a target analyte in a test sample, comprising a lateral flow assay device wherein a liquid permeable membrane (porous membrane) is used, wherein said membrane contains a test zone (detection zone) and at least one calibration zone(s) (see p4, lines 29-30 and p5, lines 1-20). The membrane also utilizes an analyte detection agent (detection probe) comprising a specific binding partner and an associated label (see p7, lines 25-29 in particular). The test zone (detection zone) utilizes an immobilized analyte receptor (capture reagent) that can bind with the analyte and/or analyte detection agent (detection probe) and generate a detectable signal. The calibration zone includes an immobilized calibration agent receptor that binds to the specific binding partner found on the analyte detection agent (detection probe) or calibration agent (calibration probe) and further, the binding of the agent to the calibration zone produces a calibration signal that is used to calibrate the signal produced in the test zone (detection signal) (see p5, lines 10-20 and p9, lines 13-19 in particular). Therefore, the lateral flow membrane, containing the analyte detection agent (detection probes), is contacted with the test

sample; the analyte detection agent (detection probes) binds to the target analyte and flows to the test zone (detection zone) wherein it binds to an immobilized analyte receptor, and generates a signal, which is detected and measured, thus providing the amount of analyte in the test sample, which is proportional to the intensity of the signal at the test zone (detection signal) calibrated by the intensity of the calibration signal (see p18-20 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al. and Klimant a calibration zone as taught by Rylatt et al. because Rylatt et al. teach the benefit of including a calibration zone with a test zone on a lateral flow assay device in order to provide accurate quantitative determination of a target analyte in a test sample, because the signal produced in the calibration zone is utilized to calibrate the signal produced in the test zone.

Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. (US 2002/0004246) in view of Klimant (US 6,770,220) and Rylatt et al. (WO 97/009620), as applied to claim 85 above, and further in view of Jou et al. (US 5,670,381).

The Daniels et al., Klimant, and Rylatt et al. references discussed above fail to teach that the capture reagent included in the calibration zone comprises a polyelectrolyte.

Jou et al. teach a device for performing an assay comprising a porous material containing a capture or reaction zone with an immobilized capture reagent. The device utilizes a specific binding member attached to a charged substance that is contacted with an analyte of interest to form a complex. The complex binds to the immobilized capture reagent in the capture or reaction zone through ion-capture, wherein the capture reagent is oppositely charged with respect to the charged substance of the analyte complex. The capture reagent preferably comprises an anionic or cationic polymeric substance (polyelectrolyte), which enables the production of a generic solid phase device for use in specific binding assays. Assay procedures for many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices. Further, the ion-capture technique increases the potential number of complexes that can be immobilized on the solid support (see column 6, lines 25-40; column 7, lines 1-46; column 10, lines 63-65; column 19, lines 29-67; column 22, lines 29-67; and column 23, lines 1-26).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to include with the detection method of Daniels et al., Klimant and Rylatt et al. a polyelectrolyte as the capture reagent in the control region (calibration zone) as taught by Jou et al. because Jou et al. teach the benefit of using an anionic or cationic polymeric substance as the immobilized capture reagent in a capture zone because the polymeric substance allows for the binding of a conjugated substance

Art Unit: 1641

or complex to a solid phase support material through ion-capture, which increases the potential number of complexes that can be immobilized on the solid support and allows for the production of a generic solid phase device, wherein many different analytes can use the same solid phase material which contains a predetermined zone of anionic or cationic capture polymer rather than an immobilized binding member capable of binding only a specific analyte as found in conventional flow-through or test-strip devices.

Conclusion

No claims are allowed.

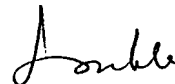
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacqueline DiRamio whose telephone number is 571-272-8785. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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